Journal of Exposure Analysis and Environmental Epidemiology 2000 10, 126–135
© 2000 Nature America, Inc. All rights reserved 1053-4245/00/$15.00
www.nature.com/jea

The German Environmental Survey 1990/1992 (GerES II): cadmium in blood, urine and hair of adults and children

KURT HOFFMANN, KERSTIN BECKER, CHRISTIAN FRIEDRICH, DIETER HELM, CHRISTIAN KRAUSE AND BERND SEIFERT

Federal Environmental Agency, Institute for Water, Soil and Air Hygiene, Berlin, Germany

As a follow-up of an earlier population study carried out in West Germany in 1985/1986 (GerES I), a nationwide Environmental Survey was conducted in Germany in 1990–1992 (GerES II). It was the aim of these studies to obtain representative data on the population's body burden and the quality of their indoor environment and immediate surroundings. The present paper reports on cadmium levels in blood, urine and hair of 4021 adults aged 25–69 and 736 children aged 6–14. The statistical analysis included both descriptive and inferential methods. The data were classified according to social factors, lifestyle characteristics, and environmental exposures. Moreover, regression analysis was used to determine the predictors of cadmium concentrations in the types of sample studied. Active cigarette smoking was found to be dominant in affecting blood and urine cadmium levels in adults, but less important for cadmium levels in hair. Age and creatinine level in urine were additional important factors influencing the cadmium concentration in urine, especially in women. Environmental and occupational exposures to cadmium played only a minor role in the exposure models for German adults. The cadmium concentration in blood and urine was generally lower in children than in adults, while no significant difference for cadmium in hair could be detected. The cadmium concentrations in all three samples were significantly higher in East German children than in West German children. *Journal of Exposure Analysis and Environmental Epidemiology* (2000) **10**, 126–135.

Keywords: *adults, blood, cadmium, children, GerES, German Environmental Survey, human biomonitoring, multiple regression model, urine.*

Introduction

Due to its toxic properties, cadmium is one of the heavy metals that are often analysed in biological samples. Data on the exposure to cadmium in the human population are necessary for the evaluation of risks to human health. Consequently, in the second German Environmental Survey (GerES II) — a nationwide representative multi-pollutant epidemiological and environmental study with about 5000 subjects selected at random and distributed over 150 sample points, which was carried out in the years 1990 to 1992 (see Krause et al., 1996a,b; Seifert et al., 2000) — samples were also analysed for their cadmium content.

Pursuing the work started with GerES I (Krause et al., 1989), the main objectives of GerES II were to establish reference values with regard to the existing body burden and the pollution of the domestic environment, to compare the exposure of children with that of adults, and to indicate whether there are differences in exposure between West and East Germany. In addition, it was the aim of the study to investigate the influence of social factors, lifestyle characteristics and the environment on the exposure to various pollutants by the use of multiple regression models.

In GerES II, cadmium levels were determined in different types of matrices: biological samples like blood, urine and hair, house dust in vacuum cleaner bags, dust deposition indoors and outdoors, tap water, and food. This paper reports the results of cadmium determination in blood, urine and hair samples. Blood cadmium level was used as an indicator of recent exposure, whereas urinary cadmium excretion was considered to reflect chronic or past exposure. The cadmium concentration in scalp hair was analysed to examine whether the determinants of cadmium level in hair are different from those in blood and urine.

Subjects and methods

Subjects and Study Area

Following a first Environmental Survey carried out in the Federal Republic of Germany in 1985/1986 (GerES I; see Krause et al., 1989), the Environmental Survey was conducted in the west of Germany (the FRG before reunification) in 1990/1991 (GerES IIa) and extended to

1. Abbreviations: CI, confidence interval; GerES, German Environmental Survey; GM, geometric mean; LOQ, limit of quantification; WHO, World Health Organization.

2. Address all correspondence to: Dr. Kerstin Becker, Federal Environmental Agency, P.O. Box 330022, 14 191 Berlin, Germany. Tel.: (49)30-8903-1311. Fax: (49)30-8903-1830.
E-mail: kerstin.becker@uba.de

Received 15 April 1999; accepted 29 December 1999.

This article is for individual use only and may not be further reproduced or stored electronically without written permission from the copyright holder.
Unauthorized reproduction may result in financial and other penalities. (c) NATURE PUBLISHING GROUP

PM3001192933

Source: https://www.industrydocuments.ucsf.edu/docs/kjwk0001

the east of Germany (former GDR) in 1991/1992 (GerES IIb).

A two-stage sampling design was applied. In the first stage, 150 sample area segments (100 in West Germany and 50 in East Germany) were selected at random. Then, in the second stage, 80 persons were randomly selected in each sample area segment. In both stages, proportionate stratification procedures were used. The strata were defined by community size in the first stage and by gender and age in the second stage (for more details, see Seifert et al., 2000).

In West Germany, 2524 adults aged 25–69 years and 453 children aged 6–14 years were investigated. In East Germany, the sample sizes for these age groups were 1497 and 283, respectively. Participation in the study was voluntary. The participation rate was 63.1% in West Germany and 69.9% in East Germany.

The participants were asked to complete questionnaires of more than 200 questions designed to obtain relevant information regarding socio-economic status, characteristics of the residential quarter, occupation, food frequencies, smoking habits, previous diseases and current health status, potential environmental exposures, household and lifestyle characteristics (Seifert et al., 2000). They were asked to collect a urine sample in the morning. A spot sample was preferred over a 24-h sample for reason of practicability. Besides the urine sample, two 5-ml samples of venous blood and a sample of approximately 200 mg scalp hair were also obtained from each subject.

Analytical Methods

Cadmium concentrations in blood were determined using an electrothermal atomic absorption spectrometer (Perkin-Elmer model 5000). Cadmium concentrations in urine were determined by Zeeman atomic absorption spectrometry (Perkin-Elmer model Z 3030). The limits of quantification (LOQs) were 0.1 μg/l for blood and 0.05 μg/l for urine. A total of 286 blood samples and 289 urine samples (6.1% in either case) showed values below LOQ. In the subsequent data treatment, the cadmium concentration of these samples was set at 0.05 and 0.025 μg/l, respectively.

All analyses were carried out under strict quality control conditions. For internal quality control concerning the analysis of blood, commercially available reference blood was used (Behringwerke, Marburg, Germany). Additionally, three further standards and three native bloods were analysed repeatedly. The coefficient of variation was between 9% and 16%. In the analysis of urine, the "Seronorm Trace Element" standard (Nycomed) was used. External quality control was achieved by regular participation in round robin tests organised by the German Society for Occupational and Environmental Medicine (for details, see Krause et al., 1996a). Here, the relative measurement error varied between 1% and 18%.

Cadmium concentrations in hair were determined by inductively coupled plasma mass spectrometry. The LOQ was 0.006 μg/g. The cadmium content of 85 hair samples (1.9%) was below LOQ. The cadmium concentration of these samples was set at 0.003 μg/g in the subsequent data treatment. For internal quality control, the reference standard GBW 09101 (Shanghai Institute of Nuclear Research, China) was used. The coefficient of variation obtained from 278 repeated measurements was 20%.

Statistical Methods

The statistical analysis included both descriptive and inferential methods. To describe the distributions of cadmium concentrations in blood, urine and hair, tables containing percentiles and geometric means (GMs) are given. Besides the 10th, 50th, and 90th percentiles, the 95th percentile was also specified to reflect the asymmetry of the distribution and to focus on persons with high exposure. Since statistical tests revealed that the data are log-normally distributed, which is in agreement with a general result concerning the distribution of environmental concentrations (Ott, 1990), the GM rather than the arithmetic mean was preferred to characterise the mean location of the data. Moreover, a 95% confidence interval for the GM (CI-GM) was added to assess the estimation error of GM. The confidence interval was obtained through the substitution method (Daly, 1998) using the confidence limits for the arithmetic mean of the logarithmically transformed data. Moreover, confidence intervals for the 95th population percentiles were calculated as 0.95 parametric confidence intervals using again a logarithmic transformation of the data (Holst and Christensen, 1992; Poulsen et al., 1997). However, these confidence intervals are not reported here to avoid confusion with the 95th percentiles of the population sample (see Krause et al., 1996a,b). In Tables 1, 3 and 5, the GM is bold-faced and specified with one more digit than the percentiles. This is warranted because of the small estimation error of the GM and the large sample size.

The data described in the tables are classified according to some variables concerning environmental exposures, lifestyle characteristics, and social factors. To check whether the mean values of the subgroups, e.g., men and women, are significantly different, the F-test of the analysis of variance is commonly used. Since the F-test is only applicable to normally distributed data, the cadmium concentrations had to be transformed logarithmically. After re-transformation, significantly different arithmetic means of the logarithmic concentrations are represented by significantly different GMs of the original concentrations. In this paper, a significance level of 0.001 is used. Therefore, the probability that the GMs are considered to be different although they are actually equal (error of the first kind) is less than or equal to 0.1%.

PM3001192934

Source: https://www.industrydocuments.ucsf.edu/docs/kjwk0001

Table 1. Cadmium concentrations (μg/l) in blood across categories of selected variables[a].

	N	P10[b]	P50	P90	P95	GM[c]	CI-GM[d]
Adults (aged 25–69 years)	3965	0.1	0.3	1.9	2.6	**0.36**	(0.35–0.38)
Smoking status							
Never-smokers	1670	0.1	0.2	0.5	0.7	**0.21**	(0.20–0.22)
Former smokers	1036	0.1	0.3	0.7	1.0	**0.25**	(0.24–0.27)
Current smokers	1258	0.3	1.3	3.0	3.7	**1.04**	(0.98–1.10)
Cigarettes smoked currently							
1–5 cigarettes/day	163	0.1	0.4	1.6	2.0	**0.42**	(0.36–0.49)
6–10 cigarettes/day	240	0.3	1.2	2.9	3.4	**1.05**	(0.94–1.18)
11–15 cigarettes/day	174	0.6	1.3	2.6	3.0	**1.20**	(1.08–1.33)
16–20 cigarettes/day	338	0.5	1.5	3.3	3.9	**1.33**	(1.21–1.45)
>20 cigarettes/day	256	0.6	1.8	3.8	5.0	**1.51**	(1.35–1.69)
Cd deposition outdoors							
≤0.25 μg/(m² day)	2325	0.1	0.3	1.8	2.5	**0.34**	(0.33–0.36)
0.26–0.5 μg/(m² day)	1075	0.1	0.3	1.9	2.6	**0.38**	(0.36–0.41)
>0.5 μg/(m² day)	565	0.1	0.4	2.0	2.8	**0.44**	(0.40–0.48)
Children (aged 6–14 years)	713	0.1	0.1	0.3	0.4	**0.14**	(0.13–0.15)
Part of the country							
West Germany	512	0.1	0.1	0.3	0.3	**0.13**	(0.12–0.14)
East Germany	201	0.1	0.2	0.4	0.5	**0.17**	(0.15–0.18)

[a]All selected variables define subgroups with significantly different geometric means ($p \leq 0.001$).
[b]Pn = nth percentile of the empirical distribution.
[c]Geometric mean.
[d]95% confidence interval for the geometric mean.

For classification of the data, only such variables were used in the tables which define subgroups with significantly different GMs of cadmium concentration. Some additional variables with subgroups of significantly different GM cadmium concentration are mentioned in the text. For a complete presentation of the results, the reader is referred to more detailed works (Krause et al., 1996a,b).

To study multivariate associations between cadmium levels and a number of other parameters that were measured, and information available from the questionnaires, regression analysis was applied. Prior to regression analysis, the cadmium concentrations were transformed using a logarithmic function. Stepwise regression was used as variable selection procedure. Following stepwise regression, predictors that accounted for less than 0.3% of the observed variance of the dependent variable were omitted in order to achieve a higher robustness and stability of the model. In this paper, the predictors of the regression model are finally obtained and their variance components are given. The variance component belonging to a certain predictor is the percentage of the total variance of cadmium concentration that is explained by the predictor. The model equations, correlations, standardised regression parameters, confidence intervals for all model parameters, and the exact definitions of all variables used are presented in an extensive report (Hoffmann et al., 1999).

Although in the study design a two-stage proportionate stratification procedure was applied to obtain a study population representative of community size, gender and age, the relative frequencies of, e.g., men and women, in the population sample were not fully identical with those of the German population. To compensate for this bias, which can partly be attributed to a less than 100% participation rate, the proportions were adjusted for the descriptive statistical analysis by weighting the data. The weighting procedure also included a correction factor for the ratio of the number of subjects from West and East Germany in the sample. The weights were used in the estimation of the parameters given in Tables 1, 3 and 5, but not in the regression analyses.

The statistical analyses were carried out under the assumption that the sample was a simple random one although the observations are clustered by sample area segments. However, the design effect (Callahan et al., 1995) of GerES II was found to be 1.05 (Seifert et al., 2000), which is close to 1. Therefore, the standard errors, confidence intervals, and test statistics used in the statistical calculations are only slightly influenced by clustering effects. Moreover, further regression analyses carried out using each sample area segment as an additional dichotomous predictor showed no significant improvements of the models derived for the cadmium concentration in blood, urine, and hair.

PM3001192935

Source: https://www.industrydocuments.ucsf.edu/docs/kjwk0001

Results

Blood Cadmium Concentrations in Adults

Table 1 describes blood cadmium concentrations in adults in relation to smoking status and smoking intensity, and cadmium deposition outdoors. Current smokers had, on average, five times higher levels than never-smokers and four times higher levels than former smokers. The cadmium concentration in blood increased significantly with increasing number of cigarettes smoked per day (for a model computation, see Figure 1 in Hoffmann et al., 2000). In contrast, the number of cigars, small cigars and pipes smoked did not influence the concentration. Although the blood cadmium concentration increased significantly with increasing duration of smoking, the long-term influence of smoking is less pronounced. This is consistent with the fact that the blood cadmium concentration reflects rather the current level of exposure than the past exposure to this metal (WHO, 1992).

The influence of environmental cadmium on the blood concentration becomes visible if the cadmium levels in blood are classified according to cadmium deposition outdoors as measured at the respective sample point over 1 year. Obviously, the influence of environmental cadmium exposure on the blood cadmium level is not as pronounced as that of current smoking. Other regional variables, like the community size or the fact of living in an urban area (yes/no), took no effect on exposure to cadmium.

Moreover, the cadmium concentration was not significantly influenced by age and gender. The GMs differed only slightly between men and women (GM=0.38 μg/l for men, GM=0.35 μg/l for women). On the other hand, bivariate statistical analyses indicated that alcohol consumption as well as the level of education had significant associations with the cadmium concentration in blood (Krause et al., 1996a). Most probably, these associations are confounder effects since the results of multivariate statistical analysis (*cf.* Table 2) showed that alcohol consumption and the level of education are negligible predictors of the cadmium concentration in blood as soon as cigarette smoking is already considered in the model.

The most important determinant of blood cadmium concentration in adults is smoking cigarettes. A specific indicator I_B for smoking habits was derived from a mathematical model which takes into account the biological half-time of cadmium in blood. In the model, the effect on the current blood cadmium level of the cigarettes smoked t months ago was characterised by a exponential function e^{-bt}. Substituting parameter b by $-\ln(0.5)/\tau$, the effect is given by $0.5^{t/\tau}$. Since the effect is reduced by half if t increases from 0 to τ, the parameter τ is the biological half-time in months (Hoffmann et al., 1999, 2000). Integrating over the entire exposure time, the indicator I_B is defined by:

$$I_B = \left[0.5^{b/3} - 0.5^{a/3}\right] * \ln(z+1).$$

In this equation, a represents the number of months since the beginning of smoking (a=0 for never-smokers), b represents the number of months since the end of smoking (b=0 for smokers and also for never-smokers, because of $b \leq a$), and the constant 3 is the estimated biological half-time. Parameter z represents the number of cigarettes usually smoked per day for both current and former smokers (z=0 for never-smokers). Hence, the indicator simultaneously includes information on the number of cigarettes smoked per day, the duration of smoking and the time since a former smoker stopped smoking. A high value of I_B means that there must have been intensive smoking during the last year, whereas having smoked several years ago has only a small effect on the value of I_B due to the relatively short biological half-time of cadmium in blood.

Besides the main influence of smoking taken into account by the indicator for smoking habits, regression analysis demonstrated that the duration of smoking has an additional influence. This additional influence was different for men and women. Furthermore, regression analysis

Table 2. Predictors of cadmium concentration in blood.

Adults (N=3791)		Children (N=703)	
Predictor	Percentage[a]	Predictor	Percentage
Indicator I_B for smoking habits[b] (West[c])	27.0	Currently smoking (0=no, 1=yes)	5.6
Indicator I_B for smoking habits (East[c])	19.3	Part of the country (0=West, 1=East)	4.3
Duration of smoking in years (men[c])	6.5	Living in urban area (0=no, 1=yes)	2.3
Sum of the duration of smoking and age in years (women[c])	1.9	Time of the year (0=May to September, 1=October to April)	1.5
	54.7		13.7

[a]Percentage of the variance of cadmium levels explained by the predictor.
[b]For definition of indicator I_B, see text.
[c]Predictor variable is defined for the subsample designated in parentheses and zero, otherwise.

PM3001192936

Source: https://www.industrydocuments.ucsf.edu/docs/kjwk0001

showed that independent of smoking, the blood cadmium level in women increased with age, while no age-related increase occurred in men. Smoking behaviour, age and gender explained 54.7% of the total variance of blood cadmium concentration in adults.

Blood Cadmium Concentrations in Children

Cadmium concentrations in children were substantially lower than in adults, even if compared with never-smokers. In children, the only significant difference in blood cadmium concentrations was between West and East Germany (Table 1).

Regression analysis showed that current smoking, the fact of living in an urban area, and the time of the year all contributed to the cadmium concentration in children's blood (Table 2). Compared with the result for adults, the regression model for children explained much less of the total variance of blood cadmium concentration, namely only 13.7%. This can partly be explained by the smaller total variability of blood cadmium concentration in the case of children as can be seen by the percentiles in Table 1.

Urinary Cadmium Concentrations in Adults

The distribution of urinary cadmium concentrations in German adults is described in Table 3, across categories of selected variables. The mean cadmium level in smokers was almost twice as high as in non-smokers. Persons aged 60–69 years had also levels twice as high as persons aged 25–29 years. Clearly, this is not a pure age-related effect, since for smokers, the duration of smoking increases with increasing age. In the present study, the urinary cadmium concentration was also significantly influenced by the community size, the level of education, occupational

Table 3. Cadmium concentrations ($\mu g/l$) in urine across categories of selected variables[a].

	N	P10[b]	P50	P90	P95	GM[c]	CI-GM[d]
Adults (aged 25–69 years)	4002	0.09	0.30	0.92	1.27	**0.287**	(0.279–0.295)
Age							
25–29 years	539	0.06	0.21	0.53	0.74	**0.189**	(0.174–0.204)
30–39 years	951	0.08	0.25	0.73	0.95	**0.247**	(0.233–0.261)
40–49 years	829	0.10	0.32	0.91	1.19	**0.297**	(0.279–0.316)
50–59 years	943	0.11	0.34	1.14	1.48	**0.342**	(0.322–0.363)
60–69 years	740	0.12	0.38	1.11	1.42	**0.363**	(0.341–0.387)
Smoking status							
Never-smokers	1689	0.08	0.24	0.65	0.90	**0.226**	(0.216–0.236)
Former smokers	1052	0.09	0.29	0.76	1.09	**0.273**	(0.259–0.288)
Current smokers	1260	0.13	0.44	1.29	1.65	**0.412**	(0.392–0.434)
Duration of smoking (current smokers)							
≤10 years	166	0.08	0.24	0.70	0.95	**0.228**	(0.199–0.262)
11–15 years	238	0.12	0.32	0.69	0.90	**0.289**	(0.262–0.320)
16–20 years	233	0.13	0.44	1.18	1.61	**0.410**	(0.364–0.461)
>20 years	610	0.16	0.60	1.54	1.91	**0.553**	(0.516–0.593)
Cd deposition outdoors							
≤0.25 $\mu g/(m^2\ day)$	2351	0.09	0.28	0.87	1.20	**0.268**	(0.258–0.278)
0.26–0.5 $\mu g/(m^2\ day)$	1085	0.10	0.31	0.91	1.27	**0.301**	(0.285–0.318)
>0.5 $\mu g/(m^2\ day)$	566	0.12	0.37	1.14	1.36	**0.348**	(0.323–0.375)
Children (aged 6–14 years)	732	<0.05	0.10	0.21	0.27	**0.087**	(0.082–0.092)
Part of the country							
West Germany	525	<0.05	0.09	0.18	0.24	**0.077**	(0.072–0.082)
East Germany	208	<0.05	0.13	0.28	0.39	**0.119**	(0.107–0.133)
Gender							
Boys	377	<0.05	0.09	0.19	0.24	**0.078**	(0.072–0.084)
Girls	355	<0.05	0.11	0.24	0.30	**0.098**	(0.090–0.106)

[a]All selected variables define subgroups with significantly different geometric means ($p \leq 0.001$).
[b]*Pn=nth* percentile of the empirical distribution.
[c]Geometric mean.
[d]95% confidence interval for the geometric mean.

PM3001192937

Source: https://www.industrydocuments.ucsf.edu/docs/kjwk0001

Table 4. Predictors of cadmium concentration in urine.

Adults (N=3827)		Children (N=731)	
Predictor	Percentage[a]	Predictor	Percentage
Indicator I_U for smoking habits[b] (men[c])	11.2		
Indicator I_U for smoking habits (women[c])	2.3		
Cigarettes smoked currently (West[c])	2.2		
Cigarettes smoked currently (East[c])	2.6		
Age (men[c])	3.2	Gender (0=boys, 1=girl)	2.2
Age (women[c])	4.1		
Creatinine level (men[c])	4.7	Creatinine level	13.4
Creatinine level (women[c])	8.5		
Part of the country (0=West, 1=East)	1.2	Part of the country (0=West, 1=East)	6.7
Cd deposition outdoors	0.7	Cd deposition outdoors	0.6
Working in workshops and warehouses frequently (0=no, 1=yes)	0.4		
	41.1		22.9

[a]Percentage of the variance of cadmium levels explained by the predictor.
[b]For definition of indicator, I_U see text.
[c]Predictor variable is defined for the subsample designated in parentheses and zero, otherwise.

activities, consumption of wine and sparkling wine, consumption of raw vegetables, and sporting activity (Krause et al., 1996a). Since the latter variables were negligible as predictors of urinary cadmium concentration in a multivariate regression model, they were not used in Table 3.

The determinants of cadmium concentration in urine were more complex than those in blood (Table 4). Again, smoking was the most important factor to have an influence on the body burden of cadmium. A total of 18.3% of the variance of urinary cadmium concentration was explained by predictors concerning smoking. In analogy to the model for cadmium in blood, a specific indicator I_U for smoking habits was used (Hoffmann et al., 1999). I_U is defined in the same way as I_B with the one exception that the constant, 3, representing an estimate of the biological half-time was replaced by 360. Thus, the indicator I_U reflects rather the long-term influence of smoking.

The level of creatinine, which expresses urine concentration, ranked second in importance. The high variance component of 13.2% can be explained by the kind of urine sample and should be reduced if a 24-h sample is used instead of a spot sample. To eliminate the influence of the creatinine level on a substance level, the substance level is sometimes divided by the creatinine level before carrying out the statistical analyses. However, in the case of the morning urine sample in GerES II, the division of cadmium concentration by the creatinine level showed no expected effect since the creatinine level remained an important factor in the regression model.

A further important factor that has an impact on the cadmium concentration in urine was found to be age (7.3%). Gender-specific differences were observed for all of the three important factors. Finally, regional and occupational variables accounted for 1.9% and 0.4% of the observed variance, respectively. Altogether, 41.1% of the observed variance could be explained by the model.

Urinary Cadmium Concentrations in Children

Urinary cadmium concentrations in children were substantially lower than in adults. The levels were, on average, 50% higher in East German children than in West German children (Table 3), a regional effect similar to the one found for blood. However, in contrast to blood, the mean urinary cadmium concentration in girls was significantly higher than in boys.

Regression analysis showed that besides the part of the country and gender, the creatinine level in urine and the cadmium deposition outdoors were further determinants (Table 4). A total of 22.9% of the observed variance could be explained.

Cadmium Concentrations in the Hair of Adults

The distribution of cadmium concentrations in hair is described as dependent on the part of country, gender, cadmium concentration in tap water, smoking status and permanent waves in the hair (Table 5). Adults in East Germany had about 50% higher cadmium levels than adults in West Germany. The cadmium concentrations in hair of men were significantly higher than those in hair of women. If subjects with chemical treatment of the hair (permanent wave, dying, tinting) are excluded, the gender-related effect is even more pronounced since the GM of cadmium concentration in women decreases to 0.33 μg/g, whereas the mean concentration in men remains unchanged (Krause et al., 1996b). The effect of permanent wave treatment is

PM3001192938

Source: https://www.industrydocuments.ucsf.edu/docs/kjwk0001

Table 5. Cadmium concentrations (μg/g) in hair across categories of selected variables[a].

	N	P10[b]	P50	P90	P95	GM[c]	CI-GM[d]
Adults (aged 25–69 years)	3725	0.02	0.04	0.16	0.27	**0.046**	(0.045–0.048)
Part of the country							
West Germany	2962	0.02	0.04	0.13	0.22	**0.042**	(0.041–0.044)
East Germany	762	0.02	0.06	0.28	0.47	**0.064**	(0.059–0.069)
Gender							
Men	1809	0.02	0.05	0.20	0.34	**0.052**	(0.050–0.055)
Women	1916	0.02	0.04	0.13	0.20	**0.041**	(0.040–0.043)
Cd in tap water							
≤0.05 μg/l	1265	0.02	0.04	0.15	0.28	**0.043**	(0.041–0.045)
0.06–0.5 μg/l	2085	0.02	0.04	0.15	0.25	**0.045**	(0.044–0.047)
>0.5 μg/l	375	0.02	0.06	0.26	0.38	**0.065**	(0.058–0.072)
Smoking status							
Non-smokers	2565	0.02	0.04	0.15	0.26	**0.044**	(0.042–0.046)
Current smokers	1159	0.02	0.05	0.18	0.32	**0.052**	(0.049–0.055)
Hair with permanent waves (women)							
No	903	0.01	0.03	0.09	0.15	**0.033**	(0.032–0.035)
Yes	998	0.02	0.05	0.16	0.25	**0.050**	(0.047–0.053)
Children (aged 6–14 years)	704	0.01	0.05	0.19	0.30	**0.048**	(0.044–0.052)
Part of the country							
West Germany	509	0.01	0.04	0.16	0.25	**0.042**	(0.038–0.047)
East Germany	196	0.02	0.06	0.27	0.41	**0.065**	(0.056–0.074)
Gender							
Boys	363	0.01	0.06	0.23	0.32	**0.056**	(0.050–0.063)
Girls	342	0.02	0.04	0.11	0.25	**0.040**	(0.036–0.044)
Cd in tap water							
≤0.05 μg/l	231	0.01	0.04	0.12	0.22	**0.037**	(0.032–0.042)
0.06–0.5 μg/l	403	0.02	0.05	0.20	0.32	**0.052**	(0.047–0.058)
>0.5 μg/l	70	0.02	0.07	0.29	0.40	**0.066**	(0.049–0.091)
Physical exercise outdoors							
Rather rarely	119	0.01	0.03	0.10	0.17	**0.035**	(0.029–0.042)
Rather frequently	583	0.02	0.05	0.21	0.30	**0.051**	(0.046–0.055)
Time of the year							
October to April	455	0.01	0.04	0.14	0.27	**0.040**	(0.036–0.045)
May to September	250	0.02	0.06	0.23	0.33	**0.065**	(0.057–0.073)

[a]All selected variables define subgroups with significantly different geometric means ($p \leq 0.001$).
[b]P*n*=*n*th percentile of the empirical distribution.
[c]Geometric mean.
[d]95% confidence interval for the geometric mean.

possibly due to a change of the sorption characteristics of the hair.

Using multivariate regression analysis, the variables discussed above were confirmed as predictors of cadmium in hair. Moreover, some minor determinants were identified. A long stay outdoors or in factories, a high maximum temperature of the day of sampling, and a high cadmium concentration in house dust as well as sparse hairs were determined as additional causes for an increased cadmium level in hair (Table 6). Altogether, 15.0% of the observed variance could be explained by the model.

Cadmium Concentrations in the Hair of Children

Cadmium concentrations in the hair of children did not differ considerably from those in hair of adults. Also, they were influenced by similar factors. Therefore, the classification in Table 5 was widely similar for both adults and children. The difference between East and West Germany found for adults was also observed for children and almost identical in magnitude: children in East Germany had about 50% higher cadmium levels in hair than children in West Germany. Cadmium in tap water seems to have a similar influence on the cadmium concentration in hair for both

PM3001192939

Source: https://www.industrydocuments.ucsf.edu/docs/kjwk0001

Table 6. Predictors of cadmium concentration in hair.

Adults (N=3592)		Children (N=695)	
Predictor	Percentage[a]	Predictor	Percentage
Part of the country (0=West, 1=East)	3.8	Part of the country (0=West, 1=East)	3.9
Gender (0=women, 1=men)	2.0	Gender (0=girls, 1=boy)	1.7
Cd in tap water	1.1	Cd in tap water	4.0
Duration of staying outdoors and in factories	3.1	Physical exercise outdoors (0=no, 1=yes)	1.5
		Intensive contact with playground sand (0=no, 1=yes)	0.9
Maximum temperature of the day	0.9	Time of the year (0=May to September, 1=October to April)	4.5
Current smoker (0=no, 1=yes)	0.7		
Cd in dust from vacuum cleaner bag	1.1		
Permanent waves in hair (0=no, 1=yes)	1.1		
Sparse hair (0=no, 1=yes)	1.2		
	15.0		16.5

[a]Percentage of the variance of cadmium levels explained by the predictor.

children and adults and can be interpreted as an effect of hair washing.

The results of bivariate statistical analysis were confirmed by multiple regression analysis. All five variables used for classification in Table 5 were predictors in the final regression model. Intensive contact with playground sand was identified as a further, yet minor, determinant. Altogether, 16.5% of the total variance of cadmium concentration in hair could be explained.

Discussion

In agreement with the findings of other studies (Watanabe et al., 1983; Ewers et al., 1985; Grasmick et al., 1985; Hahn et al., 1987; Pocock et al., 1988; Staessen et al., 1990; Ducoffre et al., 1992; Sartor et al., 1992; Alessio, 1993; Hovinga et al., 1993; Benedetti et al., 1994), the results of the statistical analysis of the GerES data demonstrate that active cigarette smoking is the main determinant of blood and urine cadmium concentration in adults.

There is a short-term and a long-term influence of smoking. Blood cadmium level is mainly determined by recent smoking since the biological half-time of cadmium in blood is only approximately 3 months (Järup et al., 1983; WHO, 1992). Beyond the effect of recent smoking, inhaled cadmium can partly be retained in the body and re-enters the vascular system years later. This explains an additional minor long-term influence of smoking which is considered in the regression model by choosing the duration of smoking as a predictor. For cadmium concentration in urine, the long-term influence is of greater relevance than the short-term influence.

The urinary cadmium level reflects the body burden. It is mostly affected by past smoking since the biological half-time of cadmium in the liver and kidney, and in other compartments is between 7 and 30 years. However, it can also be influenced by current excessive smoking. In cases where the cadmium concentration in the renal cortex tends to plateau, cadmium that is still absorbed cannot be further retained in the kidney and is rapidly excreted via the urine (WHO, 1992). This explains why the number of cigarettes smoked currently is a predictor in the regression model for cadmium concentration in urine.

Smoking cigars, small cigars and pipes does not lead to increased cadmium levels in blood and urine. Obviously, much less tobacco smoke is inhaled in these cases than in cigarette smoking. Passive smoking does not seem to be relevant for cadmium intake: surrogate parameters for passive smoking, like the frequency of staying in smoky rooms, being married to a smoker (yes/no) and the number of smokers in a household, do not influence the cadmium level significantly.

No other pathway of exposure to cadmium has an importance similar to that of smoking. This is especially true for oral exposure. According to Elinder et al. (1994), a person ingests 10–25 μg cadmium per day. In GerES IIa, the oral uptake (GM) was found to be 7.4 μg Cd/day (Becker et al., 1996). Although this is more cadmium than a heavy smoker would inhale daily (about 4 μg, assuming 20 cigarettes per day and 0.2 μg Cd per cigarette; see Elinder et al., 1983; Watanabe et al., 1987), the respective dose from oral exposure is only 5%, which is much less than the dose from exposure via inhalation (almost 50%). Indeed, ingested cadmium is absorbed less readily than inhaled cadmium (Friberg et al., 1986). It is

PM3001192940

Source: https://www.industrydocuments.ucsf.edu/docs/kjwk0001

nevertheless surprising that an effect of special food consumption, e.g., frequent offal and fish meals, could not be detected by the descriptive and inferential statistical analysis carried out. However, it should be noted that in a specific comparative study, Hovinga et al. (1993) could demonstrate a slight influence of fish consumption on the blood cadmium level.

Occupational exposure is not important as far as an effect on the mean cadmium level in the general population is concerned. Out of the occupational variables, only "frequently working in workshops and warehouses" (yes/no) was proven to be a minor predictor of urinary cadmium concentration in adults. Although specific information about cadmium exposure at work was available from the questionnaires, the relative small number of subjects with a known occupational exposure to cadmium, namely 21 out of 4021 adults, allows no detection of significant differences. In fact, such differences could be observed in specific studies carried out to examine associations between occupational exposure and cadmium level in blood and urine (Järup et al., 1983; Kawada et al., 1990; Karakya et al., 1993).

In contrast to adults, much less is known about determinants of blood and urine cadmium concentration in children. The levels in children are substantially lower and vary less than in adults. Therefore, measurement errors are of relatively greater importance and may account for the lower percentage of variance explained in the regression models for children. Moreover, active cigarette smoking as the main determinant of cadmium level in adults is of minor relevance for children.

Determinants of cadmium concentration in hair are somewhat different from those relevant for blood and urine. Outdoor activities, chemical treatment of the hair, and the cadmium concentration in tap water are specific predictors in the model for hair. Men and boys have substantially higher cadmium levels in hair compared to women and girls, which was also found in other studies (DiPietro et al., 1989; Leotsinidis and Kondakis, 1990; Wilhelm et al., 1994). For both adults and children, there are essentially the same factors which influence the cadmium level in hair. Altogether, the degree of explanation of the variance of cadmium concentration in hair is much lower than that of the cadmium concentration in blood and urine.

The cadmium levels in East Germany are, on average, higher than in West Germany. The difference is significant for all considered matrices and for both adults and children, with the exception of blood cadmium levels in adults. A possible explanation is the different environmental exposure in both parts of Germany in the years 1990–1992 and before. The soil cadmium pollution was higher in the former GDR than in West Germany. Further, the mean cadmium content in cigarettes smoked in the GDR was higher than in the old states of the Federal Republic of Germany. In another large epidemiological study with more than 2000 children at the age of 6 years carried out in West and East Germany, no regional different blood cadmium levels were found (Begerow et al., 1994). Obviously, regional different cadmium concentrations only appear in elder children and adults.

In addition, it should be noted that the mean cadmium concentrations in blood of West German adults were lower in GerES IIa (1990/1991) compared with GerES I which was conducted in 1985/1986 (Krause et al., 1989). The GM of the blood cadmium concentration decreased by 25% (from 0.45 to 0.36 μg/l) over the period of 5 years.

Acknowledgments

Financial support of this study by the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety is gratefully acknowledged. The authors thank M. Drews, C. Englert, U. Kortwich, H. Pick-Fuß, and L. Windmüller for skillful technical assistance.

References

Alessio L. Reference values for the study of low doses of metals. *Int. Arch. Occup. Environ. Health* 1993: 65: 23–27.

Becker K., Nöllke P., Hermann-Kunz E., Krause C., Schenker D., and Schulz C. Umwelt Survey 1990/91, Band III: Zufuhr von Spurenelementen und Schadstoffen mit der Nahrung (Duplikate und Diet History) in den alten Bundesländern (Intake of Trace Elements and Pollutants with Diet Duplicates and Diet History in West Germany). WaBoLu-Hefte 3/1996, ISSN 0175-4211. Institute for Water, Soil and Air Hygiene of the Federal Environmental Agency, Berlin, 1996.

Begerow J., Freier I., Turfeld M., Krämer U., and Dunemann L. Internal lead and cadmium exposure in 6-year-old children from western and eastern Germany. *Int. Arch. Occup. Environ. Health* 1994: 66: 243–248.

Benedetti J.L., Dewailly E., Turcotte F., and Lefebvre M. Unusually high blood cadmium associated with cigarette smoking among three subgroups of the general population, Quebec, Canada. *Sci. Total Environ.* 1994: 152: 161–167.

Callahan M.A., Clickner R.P., Whitmore R.W., Kalton G., and Sexton K. Overview of important design issues for national human exposure assessment survey. *J. of Exp. Analysis and Environ. Epid.* 1995: 5: 297–325.

Daly L.E. Confidence limits made easy: interval estimation using a substitution method. *Am. J. Epidemiol.* 1998: 147: 783–790.

DiPietro E., Phillips D.L., Paschal D.C., and Neese J.W. Determination of trace elements in human hair, reference intervals for 28 elements in non-occupationally exposed adults in the US and effects of hair treatments. *Biol. Trace Element Res.* 1989: 22: 83–100.

Ducoffre G., Claeys F., and Sartor F. Decrease in blood cadmium levels over time in Belgium. *Arch. Environ. Health* 1992: 47: 354–356.

Elinder C.G., Kjellström T., Lind B., Linnmann L., Piscator M., and Sundstedt K. Cadmium exposure from smoking cigarettes. Variations with time and country purchased. *Environ. Res.* 1983: 32: 220–227.

Elinder C.G., Friberg L., Kjellström T., Nordberg G., and Oberdoerster G.

PM3001192941

Source: https://www.industrydocuments.ucsf.edu/docs/kjwk0001

Biological monitoring of metals. Chemical Safety Monographs. WHO, Genf., 1994.

Ewers U., Brockhaus A., Dolgner R., Freier I., Jermann E., Bernard A., Stiller-Winkler R., Hahn R., and Manojlovic N. Environmental exposure to cadmium and renal function of elderly women living in cadmium-polluted areas of the Federal Republic of Germany. *Int. Arch. Occup. Environ. Health* 1985: 55: 217–239.

Friberg L., Kjellström T., and Nordberg G.F. Cadmium. In: Friberg L., Nordberg G.F., Vouk V. (Eds.), Handbook on the Toxicology of Metals, 2nd edn. Elsevier Science Publishers.

Grasmick C., Huel G., Moreau T., and Sarmini H. The combined effect of tobacco and alcohol consumption on the level of lead and cadmium in blood. *Sci. Total Environ.* 1985: 41: 207–217.

Hahn R., Ewers U., Jermann E., Freier I., Brockhaus A., and Schlipköter H.W. Cadmium in kidney cortex of inhabitants of North-West Germany: its relationship to age, sex, smoking and environmental pollution by cadmium. *Int. Arch. Occup. Environ. Health* 1987: 59: 165–176.

Hoffmann K., Helm D., Becker K., Friedrich C., Krause C., Nöllke P., Seiwert M., and Seifert B. Umwelt Survey 1990/92, Band IX: Cadmium — Zusammenhangsanalyse (Cadmium — Multivariate Statistical Analysis). WaBoLu-Hefte 1/1999, ISSN 0175-4211. Institute for Water, Soil and Air Hygiene of the Federal Environmental Agency, Berlin, 1999.

Hoffmann K., Krause C., and Seifert B. The German Environmental Survey 1990/92 (GerES II): primary predictors of blood cadmium levels in adults. *Arch. Environ. Health* 2000, submitted.

Holst E., and Christensen J.M. Intervals for the description of the biological level of a trace metal in a reference population. *The Statistician* 1992: 41: 233–242.

Hovinga M.E., Sowers M., and Humphrey H.E.B. Environmental exposure and lifestyle predictors of lead, cadmium, PCB, and DDT levels in great lakes fish eaters. *Arch. Environ. Health* 1993: 48: 98–104.

Järup L., Rogenfelt A., Elinder C.G., Nogawa K., and Kjellström T. Biological half-time of cadmium in the blood of workers after cessation of exposure. *Scand. J. Work Environ. Health* 1983: 9: 327–331.

Karakya A., Süzen S., Vural N., and Oflaz G. Evaluation of the biological threshold value of urinary cadmium concentration in a group of workers. *Bull. Environ. Contam. Toxicol.* 1993: 51: 483–489.

Kawada T., Tohyama C., and Suzuki S. Significance of the excretion of urinary indicator proteins for a low level of occupational exposure to cadmium. *Int. Arch. Occup. Environ. Health* 1990: 62: 95–100.

Krause C., Chutsch M., Henke M., Huber M., Kliem C., Schulz C., and Schwarz E. Umwelt Survey, Band I: Studienbeschreibung und humanbiologisches Monitoring (Environmental Survey, Vol. I: Study Design and Human Biomonitoring). WaBoLu-Hefte 5/1989. Institute for Water, Soil and Air Hygiene of the Federal Health Office, Berlin, 1989.

Krause C., Babisch W., Becker K., Bernigau W., Hoffmann K., Nöllke P., Schulz C., Schwabe R., Seiwert M., and Thefeld W. Umwelt Survey 1990/92, Band Ia: Studienbeschreibung und Human Biomonitoring: Deskription der Spurenelementgehalte im Blut und Urin der Bevölkerung der Bundesrepublik Deutschland (Environmental Survey 1990/92, Vol. Ia: Study Design and Human Biomonitoring: Trace Elements in Blood and Urine of the German Population). WaBoLu-Hefte 1/1996, ISSN 0175-4211. Institute for Water, Soil and Air Hygiene of the Federal Environmental Agency, Berlin, 1996a.

Krause C., Schulz C., Becker K., Bernigau W., Hoffmann K., Nöllke P., Schwabe R., and Seiwert M. Umwelt Survey 1990/92, Band Ib: Human Biomonitoring: Deskription der Spurenelementgehalte im Haar der Bevölkerung der Bundesrepublik Deutschland (Environmental Survey 1990/92, Vol. Ib: Human Biomonitoring: Trace Elements in the Hair of the German Population). WaBoLu-Heft 2/1996, ISSN 0175-4211. Institute for Water, Soil and Air Hygiene of the Federal Environmental Agency, Berlin, 1996b.

Leotsinidis M., and Kondakis X. Trace metals in scalp hair of Greek agricultural workers. *Sci. Total. Environ.* 1990: 95: 149–156.

Ott W.R. A physical explanation of the log normality of pollutant concentrations. *J. Air Waste Manage. Assoc.* 1990: 40: 1378–1383.

Pocock S.J., Delves H.T., Ashby D., Shaper A.G., and Clayton B.E. Blood cadmium of British middle-aged men. *Human. Toxicol.* 1988: 7: 95–103.

Poulsen O.M., Holst E., and Christensen J.M. International Union of Pure and Applied Chemistry (IUPAC). Calculation and application of coverage intervals for biological reference values. *Pure Appl. Chem.* 1997: 69: 1601–1611.

Sartor F.A., Rondia D.J., Claes F.D., Staessen J.A., Lauwerys R.R., Bernard A.M., Roels J.P., Bruaux P.J., Ducoffre G.M., Lijnen P.J., Thijs L.B., and Amery A.K. Impact of environmental cadmium pollution on cadmium exposure and body burden. *Arch. Environ. Health* 1992: 47: 347–353.

Seifert B., Becker K., Hoffmann K., Krause C., and Schulz C. The German Environmental Survey 1990/92 (GerES II): a representative population study. *J. of Exp. Anal. and Environ. Epid.* 2000, this issue.

Staessen J., Yeoman W.B., Fletcher A.E., Markowe H.L.J., Marmot M.G., Rose G., Semmences A., Shipley M.J., and Bulpitt C.J. Blood cadmium in London civil servants. *Int. J. Epidemiol.* 1990: 19: 362–366.

Watanabe T., Koizumi A., Fujita H., Kumai M., and Ikeda M. Cadmium levels in the blood of inhabitants in non-polluted areas in Japan with special references to aging and smoking. *Environ. Res.* 1983: 31: 472–483.

Watanabe T., Kasahara M., Nakatsuka H., and Ikeda M. Cadmium and lead contents of cigarettes produced in various areas of the world. *Sci. Total Environ.* 1987: 66: 29–37.

WHO. Cadmium. Environmental Health Criteria 134. World Health Organization, Geneva, 1992.

Wilhelm M., Lombeck I., and Ohnesorge F.K. Cadmium, copper, lead and zinc concentrations in hair and toenails of young children and family members: a follow-up study. *Sci. Total Environ.* 1994: 141: 275–280.

PM3001192942

Source: https://www.industrydocuments.ucsf.edu/docs/kjwk0001